AMINOSYN-RF - isoleucine, leucine, lysine acetate, methionine, phenylalanine, threonine, tryptophan, valine, arginine and histidine injection, solution

HOSPIRA, INC.

R_x only

DESCRIPTION

Aminosyn®-RF 5.2%, Sulfite-Free, (an amino acid injection — renal formula) is a sterile, nonpyrogenic solution for intravenous infusion. Aminosyn-RF 5.2% is oxygen sensitive. The solution contains the following crystalline amino acids:

	mg/100 mL	Min. Daily Need (mg**)
Essential Amino Acids		
Isoleucine	462	700
Leucine	726	1100
Lysine Acetate*	535	800
Methionine	726	1100
Phenylalanine	726	1100
Threonine	330	500
Tryptophan	165	250
Valine	528	800
Nonessential Amino Acids		
Arginine	600	—
Histidine***	429	—

* Amount cited is for Lysine alone and does not include the acetate salt.

** The minimum daily quantities needed to maintain nitrogen balance in the healthy adult. (Rose, W.C., The Sequence of Events Leading to the Establishment of the Amino Acid Needs of Man, Am J. Public Health, 58:2020, 1968.)

*** Histidine is considered essential for patients in renal failure.

Electrolytes and Product Characteristics	
Aminosyn	5.2%
Acetate ($C_2H_3O_2^-$)[a] (mEq/Liter)	113
Protein Equivalent (approx. grams/liter)	52.27
Total Nitrogen (grams/liter)	7.93
Osmolarity (mOsmol/liter)	427

pH (Range)	5.2 (4.5 to 6.0[b])

[a] Includes acetate from acetic acid used in processing and from Lysine acetate.

[b] Adjusted with acetic acid.

Each 500 mL represents three Rose Units of essential amino acids plus arginine and histidine.

The formulas for the individual amino acids present in Aminosyn-RF 5.2% are as follows:

Essential Amino Acids	
Isoleucine, USP	($C_6H_{13}NO_2$)
Leucine, USP	($C_6H_{13}NO_2$)
Lysine Acetate, USP	($C_6H_{14}N_2O_2 \bullet CH_3COOH$)
Methionine, USP	($C_5H_{11}NO_2S$)
Phenylalanine, USP	($C_9H_{11}NO_2$)
Threonine, USP	($C_4H_9NO_3$)
Tryptophan, USP	($C_{11}H_{12}N_2O_2$)
Valine, USP	($C_5H_{11}NO_2$)
Nonessential Amino Acids	
Arginine, USP	($C_6H_{14}N_4O_2$)
Histidine, USP	($C_6H_9N_3O_2$)

The flexible plastic container is fabricated from a specially formulated polyvinylchloride. Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly.

Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the plastic container materials.

Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period.

CLINICAL PHARMACOLOGY

Aminosyn-RF 5.2%, Sulfite-Free, (an amino acid injection— renal formula) is a mixture of amino acids specifically designed for patients with acute renal failure who are unable to eat. The use of these essential amino acids in the management of the uremic patient is based on the minimal requirements for each of the eight amino acids essential in adult nutrition established by Rose. In renal failure nonspecific nitrogen such as urea, glycine, or ammonium chloride, are broken down in the intestine. The ammonia formed is absorbed into the portal system and incorporated by the liver into nonessential amino acids, provided requirements for essential amino acids are being met. By this metabolic route, urea nitrogen contributes to protein synthesis when the proper combination of essential amino acids, sufficient calories and other required nutrients are administered.

Thus, the administration of essential amino acids to uremic patients, particularly those who are protein-deficient, results in the utilization of retained urea in protein synthesis, and may be followed by a drop in BUN and resolution of many of the symptoms associated with azotemia.

Aminosyn-RF 5.2% contains histidine, an amino acid considered essential for infant growth, and identified as an essential amino acid for uremic patients.

In patients with potentially reversible acute renal failure who cannot eat, maintenance of adequate nutrition may assist in reducing morbidity.

INDICATIONS AND USAGE
Aminosyn-RF 5.2%, Sulfite-Free, (an amino acid injection— renal formula) is indicated only as an adjunct to management of patients with potentially reversible acute renal failure who are unable to eat. When infused with hypertonic dextrose as a source of calories and with added appropriate electrolytes and vitamins, Aminosyn-RF 5.2% is suitable as an intravenous source of protein in a parenteral nutritional regimen for such patients.

CONTRAINDICATIONS
1. Severe uncorrected electrolyte or acid-base imbalance.

2. Hyperammonemia.

3. Decreased circulating blood volume.

WARNINGS
Intravenous infusion of amino acids may induce a rise in blood urea nitrogen (BUN), especially in patients with impaired hepatic or renal function. Appropriate laboratory tests should be performed periodically and infusion discontinued or nitrogen content reduced if BUN levels continue to rise inappropriately.
Administration of nitrogen in any form to patients with marked hepatic insufficiency may result in serum amino acid imbalances or CNS complications. Aminosyn-RF 5.2%, Sulfite-Free, (an amino acid injection — renal formula), therefore, should be used with caution in such patients.
Solutions containing acetate ion should be used with great care in patients with metabolic or respiratory alkalosis.
Hyperammonemia is of special significance in infants, as it can result in mental retardation. Therefore, it is essential that blood ammonia levels be measured frequently in infants.
Aminosyn-RF 5.2% does not replace dialysis and conventional supportive therapy in patients with renal failure.
WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.
Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS
CLINICAL EVALUATIONS AND LABORATORY DETERMINATIONS, AT THE DISCRETION OF THE ATTENDING PHYSICIAN, ARE NECESSARY FOR PROPER MONITORING DURING ADMINISTRATION. Blood studies should include glucose, urea nitrogen, serum electrolytes, acid-base balance, blood ammonia levels, serum proteins, kidney and liver function tests, serum osmolality and hemogram. Circulating blood volume should be determined if indicated. If sepsis is suspected, blood cultures should be taken.
Clinically significant hypocalcemia, hypophosphatemia or hypomagnesemia may occur as a result of therapy with Aminosyn-RF 5.2%, Sulfite-Free, (an amino acid injection — renal formula) and hypertonic dextrose; electrolyte replacement may become necessary.
In order to promote urea nitrogen reutilization in patients with renal failure, it is essential to provide adequate calories with minimal amounts of the essential amino acids and to restrict the intake of nonessential nitrogen. Hypertonic dextrose solutions are a convenient and metabolically effective source of concentrated calories. Special care must be taken when giving hypertonic glucose to provide calories in diabetic or prediabetic patients. Hypertonic solutions should be administered through an indwelling catheter with the tip located in the superior vena cava. When abrupt cessation of hypertonic dextrose is required, monitoring for rebound hypoglycemia should be instituted. Essential fatty acid deficiency (EFAD) is becoming increasingly recognized in patients on long term TPN (more than 5 days). The use of fat emulsion to provide 4–10% of total caloric intake as linoleic acid may prevent EFAD.
Fluid balance should be carefully monitored in patients with renal failure to avoid excessive fluid overload, especially in relation to cardiac insufficiency.

SPECIAL PRECAUTIONS FOR CENTRAL INFUSIONS
ADMINISTRATION BY CENTRAL VENOUS CATHETER SHOULD BE USED ONLY BY THOSE FAMILIAR WITH THIS TECHNIQUE AND ITS COMPLICATIONS.

Central vein infusion (with added carbohydrate solutions) of amino acid solutions requires a knowledge of nutrition as well as clinical expertise in recognition and treatment of complications. Attention must be given to solution preparation, administration and patient monitoring. IT IS ESSENTIAL THAT A CAREFULLY PREPARED PROTOCOL, BASED ON CURRENT MEDICAL PRACTICES, BE FOLLOWED, PREFERABLY BY AN EXPERIENCED TEAM.
SUMMARY HIGHLIGHTS OF COMPLICATIONS
(Also see Current Medical Literature)

1. **Technical**
   The placement of a central venous catheter should be regarded as a surgical procedure. X-ray is the best means of verifying catheter placement. Complications known to occur from the placement of central venous catheters are pneumothorax, hemothorax, hydrothorax, artery puncture and transection, injury to the brachial plexus, malposition of the catheter, formation of arteriovenous fistula, phlebitis, thrombosis and air and catheter emboli.

2. **Septic**
   The risk of sepsis is present constantly during administration of total parenteral nutrition. It is imperative that the preparation of the solution and the placement and care of catheters be accomplished under strict aseptic conditions.
   Solutions should ideally be prepared in the hospital pharmacy under a laminar flow hood using careful aseptic technique to avoid inadvertent touch contamination. Solutions should be used promptly after mixing. Storage should be under refrigeration and limited to a brief period of time, preferably less than 24 hours.

3. **Metabolic**
   A wide variety of metabolic complications can occur during total parenteral nutrition and frequent evaluations are necessary, especially during the first few days of administration.

Pregnancy Category C
Animal reproduction studies have not been conducted with Aminosyn-RF 5.2%. It is also not known whether Aminosyn-RF 5.2% can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Aminosyn-RF 5.2% should be given to a pregnant woman only if clearly needed.

Geriatric Use
Clinical studies of Aminosyn-RF have not been performed to determine whether patients over 65 years respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, dose selection for elderly patients should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. This drug is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal functions.
Aminosyn 5.2% contains no more than 25 mcg/L of aluminum.
SPECIAL PRECAUTIONS IN PATIENTS WITH RENAL INSUFFICIENCY
Frequent laboratory studies are necessary in patients with renal insufficiency. In renal failure hyperglycemia may not be reflected by glycosuria. Blood glucose must be determined frequently, often every six hours to guide dosage of dextrose, and insulin should be given, if required.

SPECIAL PRECAUTIONS IN PEDIATRIC PATIENTS
Aminosyn-RF 5.2%, Sulfite-Free, (an amino acid injection— renal formula) should be used with special caution in pediatric patients with acute renal failure, especially low birth weight infants. Laboratory and clinical monitoring of pediatric patients, especially those who are nutritionally depleted, must be extensive and frequent. See **Children** section under **DOSAGE AND ADMINISTRATION** for additional information.
Frequent monitoring of blood glucose is required in low birth weight or septic infants as hypertonic dextrose infusion involves a greater risk of hyperglycemia in such patients.

ADVERSE REACTIONS
Adverse effects include metabolic, fluid, electrolyte and acid-base imbalances unless appropriate monitoring and corrective management are accomplished during Aminosyn-RF 5.2%, Sulfite-Free, (an amino acid injection— renal formula) therapy.

OVERDOSAGE
In the event of overhydration or solute overload, re-evaluate the patient and institute appropriate corrective measures. See WARNINGS and PRECAUTIONS.

DOSAGE AND ADMINISTRATION
Dosage
Fat emulsion coadministration should be considered when prolonged (more than 5 days) parenteral nutrition is required in order to prevent essential fatty acid deficiency (EFAD). Serum lipids should be monitored for evidence of EFAD in patients maintained on fat-free TPN.
Adults: The objective of nutritional management of renal decompensation is to provide sufficient amino acid and caloric support for protein synthesis without exceeding the renal capacity to excrete metabolic wastes.
A dosage of 2.4 to 4.7 grams of nitrogen per day (from essential amino acids) with adequate calories will maintain nitrogen equilibrium in patients with uremia. If more nitrogen and calories are required in severely stressed patients in acute renal failure

who cannot eat, higher dosages may be administered provided great care is taken to avoid exceeding limits of fluid intake or glucose tolerance.

In general, dosage should be guided by fluid, glucose and nitrogen tolerances, as well as the metabolic and clinical response. The rate of rise in BUN generally diminishes with infusion of essential amino acids. However, excessive intake of protein or increased protein catabolism may alter this response.

The usual daily dose ranges from 300 to 600 mL of Aminosyn-RF 5.2%, Sulfite-Free, (an amino acid injection— renal formula) equivalent to 2.4 to 4.7 grams of nitrogen in 15.7 to 31 grams of essential amino acids. Adequate calories should be administered simultaneously. Each 500 mL of Aminosyn-RF 5.2% mixed under sterile conditions with 832 mL of Dextrose 70% will provide a solution of 1.95% of Aminosyn-RF 5.2% in 44% dextrose. This mixture provides a calorie-to-nitrogen ratio of 504:1.

Electrolyte supplementation may be required.

Elevated phosphorus, potassium and magnesium levels generally decrease during treatment with Aminosyn-RF 5.2%. Particular care should be taken in the presence of cardiac arrhythmias or digitalis toxicity to assure that sufficient quantities of these electrolytes are provided when necessary.

Compatibility of electrolyte additives to the mixtures of Aminosyn-RF 5.2% and hypertonic dextrose must be considered and potentially incompatible ions (calcium, phosphate) may be added to alternate infusion bottles to avoid precipitation.

Children: Pediatric requirements for Aminosyn-RF 5.2% vary greatly depending upon growth, nutritional state and degree of renal insufficiency. A dosage of 0.5 to 1 gram of essential amino acids per kilogram of body weight per day will meet the requirements of the majority of pediatric patients. Initial daily dosage of Aminosyn-RF 5.2% should be low and increased slowly; more than one gram of essential amino acids per kilogram of body weight per day is not recommended. The total volume of nutritional solution and the rate at which it is administered will vary with the child's age, nutritional and growth state, as well as the degree of renal failure. See **Special Precautions in Pediatric Patients** for additional information.

Administration

Aminosyn-RF 5.2% admixed with sufficient dextrose to provide caloric energy requirements may be safely administered via a central venous catheter with the tip located in the vena cava.

Initial infusion rates should be slow, generally 20 to 30 mL/hour for the first 6 to 8 hours. Increments of 10 mL/hour for each hour are suggested up to a maximum rate of 60 to 100 mL/hour. If administration rates fall behind the scheduled 24 hour dosage, no attempt should be made to catch up to the planned intake. The patient's fluid, nitrogen and glucose tolerance should be the governing factor of the rate of administration. Uremic patients are frequently glucose intolerant especially in association with peritoneal dialysis; insulin may be required to prevent hyperglycemia. When hypertonic dextrose infusion is abruptly discontinued, rebound hypoglycemia may be prevented by administering 5% dextrose.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

WARNING: Do not use flexible container in series connections.

HOW SUPPLIED

Aminosyn-RF 5.2%, Sulfite-Free, (an amino acid injection— renal formula) is supplied in 500 mL single-dose containers (List No. 4166).

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.]**Avoid exposure to light.**

 EN-0498 Printed in USA

HOSPIRA, INC., LAKE FOREST, IL 60045 USA